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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/636,088	08/07/2003	Frank Himmelsbach	1/1386	9824

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MICHAEL P. MORRIS
BOEHRINGER INGELHEIM CORPORATION
900 RIDGEBURY ROAD
P. O. BOX 368
RIDGEFIELD, CT 06877-0368

EXAMINER	
BERCH, MARK L	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 11/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/636,088	HIMMELSBACH ET AL.	
	Examiner	Art Unit	
	Mark L. Berch	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-10 and 12-15* is/are rejected.

7)☒ Claim(s) *5 and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/18/2006 has been entered.

Applicant's request filed 07/18/2006, for suspension of action in this application under 37 CFR 1.103(c) is denied as being improper. MPEP 709 (I)(B)(1) says that the request filed with the filing of a an RCE is to use the check box provided on the transmittal form PTO/SB/29 or PTO/SB/30, or is to be submitted on a separate paper. Neither was done; the request was on the same sheet as the request for an RCE, and no PTO/SB/29 or PTO/SB/30 was used.

Attention is drawn to 20040116328, cited previously. This publication has species falling within the instant claims, see e.g. table starting on page 16, when Z1 is N and Z2 is CR2. This document does not appear to be prior art against these claims, as the translation of the provisional application appears to support the instant claims. If any material was added to claim 1 which was not present in the definition of the variables in the provisional applications, applicants are requested to point this out.

Information Disclosure Statement

The information disclosure statement filed 1/9/04 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other

information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. That is, the two references struck were not provided and hence not considered; the US patents were considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The new phrasing of "for the prevention or treatment of a disease or condition selected from the group consisting of ... allograft transplantation" makes no sense at all. Allograft transplantation is neither a disease nor a condition; it is a surgical procedure. As such, it would not be prevented or treated. It is impossible to tell what is being claimed here.

Claim 15 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or

with which it is most nearly connected, to make and/or use the invention. Treatment or prevention of rheumatoid arthritis with DPP-IV inhibitors cannot be deemed enabled. And prevention of any of these disorders except Diabetes type 2 cannot be deemed enabled either.

Pursuant to In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see In re Vaeck, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(1) Breadth of claims. Owing to the huge scope of the 4 primary variables, the claims cover trillions of compounds.

(2) The nature of the invention and predictability in the art: The invention is directed toward medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

((3) Direction or Guidance: That provided is very limited. The dosage range information on page 27 is incomplete, in that it is given in the form of mg, not mg/kg. Moreover, this is generic, the same for the many disorders covered by the specification, which are quite extensive. Thus, there is no specific direction or guidance regarding a regimen or dosage effective specifically for rheumatoid arthritis.

(4) State of the Prior Art: These compounds are 7-substituted hypoxanthines with a particular substitution pattern at the 1-position. So far as the examiner is aware, no 7-substituted hypoxanthines of any kind have been used for the treatment of rheumatoid arthritis.

(5) Working Examples: There are none, either to the treatment of RA or to any animal model for RA.

(6) Skill of those in the art: The skill level in RA is relatively low. Very few agents have been successfully used to treat RA itself, and these have all operated by the mechanism of α-TNF inhibition. There has been some research on the use of DPP-IV inhibitors for RA, but even as of 2005, after the instant filing date, the situation is still unclear. Moreover, some early positive results have recently been reassessed. In Busso et al., American Journal of Pathology 166:433-442 (2005), it is stated: "Paradoxically, although DPPIV inhibition was beneficial in experimental models of RA and multiple sclerosis, genetic deficiency of CD26 leads to exacerbation of these diseases: AIA was more severe in CD26-deficient mice (this study); similarly, EAE was exacerbated in CD26-knockout mice. The

reasons for such discrepancy may be related to the additional effects of the inhibitors, able to act even in DPPIV-deficient animals suggesting that, besides DPPIV inhibition, these inhibitors may have other functional targets." In other words, the beneficial effects seen in earlier studies are likely not to have arisen from DPPIV inhibition, but from the fact that the particular drugs used had "other functional targets." In particular, the paper goes on to suggest that the other target may be DPP8/9, i.e. that the drugs were not particular selective for DPP-IV. Thus, it is clear that, even as of 2005, it has not been established that inhibition of DPP-IV is of value in treating RA, and indeed, such a conclusion is inconsistent with the fact that AIA was more severe in CD26-deficient mice. Prevention is even a harder task. Type 1 diabetes is not even considered to be preventable by any means. (7) The quantity of experimentation needed: Owing especially to factors 1, 4, 5, and 6, the amount is expected to be high.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985);

In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 6-10, 12-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 and others of copending Application No. 11419756. Although the conflicting claims are not identical, they are not patentably distinct from each other because there is no patentable distinction between the two applications.

In claim 1 of 11419756, see choice K of page 287, which gives the phenyl-(CH2)m-A-(CH2)n- moiety. If m=0, A=carbonyl and n=1, then this is the phenylcarbonylamino group. It can be substituted by R10. On page 283, choice e, R10 can be as first choice, alkyl-carbonyl-amino. The two examples of such species are species 318 on page 256, and species 242 on page 249, which both have the acetylamino. This is virtually identical to the first R10 choice in this case, the formylamino. This differs from the claims of this case in that the 11419756 species has the C2 alkanoyl, whereas this case has the C1 alkanoyl (see e.g. species (1) of claim 6). Compounds that differ only by the presence or absence of an extra methyl group or two are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologue. As was stated in *In re Grose*, 201 USPQ 57, 63, "The known structural relationship between adjacent homologues, for example, supplies a chemical theory upon which a prima facie case of obviousness of a compound may rest." The homologue is expected to be preparable

by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methyl groups. See *In re Wood,* 199 USPQ 137; *In re Hoke,* 195 USPQ 148; *In re Lohr,* 137 USPQ 548; *In re Magerlein,* 202 USPQ 473; *In re Wiechert,* 152 USPQ 249; *Ex parte Henkel,* 130 USPQ 474; *In re Jones,* 74 USPQ 152, 154; *Ex Parte Fischer* 96 USPQ 345; *In re Fauque,* 121 USPQ 425; *In re Druey,* 138 USPQ 39; *Ex parte Fischer,* 96 USPQ 345; i*n re Bowers and Orr,* 149 USPQ 570. In all of these cases, the close structural similarity between two compounds differing by one or two methyl groups was itself sufficient show obviousness. Note also *In re Jones,* 21 USPQ2d 1942, which states at 1943 "Particular types or categories of structural similarity without more, have, in past cases, given rise to *prima facie* obviousness"; one of those listed is "adjacent homologues and structural isomers". Similar is *In re Schechter and LaForge,* 98 USPQ 144, 150, which states "a novel useful chemical compound which is homologous or isomeric with compounds of the prior art is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compounds." Note also *In re Deuel* 34 USPQ2d 1210, 1214 which states, "Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties." See also MPEP 2144.09, second paragraph.

Claims 1-4, 6-10, 12-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 and others of copending Application No. 10693069. Although the conflicting claims are not identical, they are not patentably distinct from each other because there is no patentable distinction between the two applications.

The same issues apply, as 10693069 is the daughter of 10467961.

Claims 1-4, 6-10, 12-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 and others of copending Application No. 10639036. Although the conflicting claims are not identical, they are not patentably distinct from each other because there is no patentable distinction between the two applications.

Much the same analysis occurs with 10639036 as well. Note the choice of the methylcarbonylamino substituent on the phenylcarbonylmethyl, at page 196, line 2, which is the same substituent as mentioned above. Species 96, 105, 110, 119, 147, 149 and 157 in 10639036 are thus homologs of the aforementioned species (1) of claim 6 in this case.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Objections

Claims 5 and 11 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the

grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, THIS ACTION IS MADE FINAL even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 571-272-0663. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on (571)272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark L. Berch
Primary Examiner
Art Unit 1624

10/27/06